I. AMENDMENT OF CLAIMS

This Listing of Claims will replace all prior versions and listings of claims in the application.

LISTING OF CLAIMS

Claims 1-5. (Cancelled)

Claim 6. (currently amended): A method for treating pain in humans for a time period of about 24 hours, comprising

administering to a human patient at a dosing interval of about 24 hours a solid, controlled-release oral dosage form comprising 8 to 64 mg of hydromorphone or a pharmaceutically acceptable salt thereof incorporated into a controlled-release formulation comprising a tablet overcoated with a controlled-release coating derived from an aqueous dispersion of a hydrophobic polymer selected from the group consisting of a cellulosic polymer, an acrylic polymer, and mixtures thereof,

wherein the coating has been stabilized by curing for about 24 hours or more at a temperature greater than the glass transition temperature of the hydrophobic polymer and a relative humidity from about 60% to about 100% such that the dosage form attains a dissolution profile which is substantially unaffected by exposure to storage conditions of at least one month at a temperature of 40°C and a relative humidity of 75%,

wherein (i) the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C, is such that from 12.5% to 42.5% (by wt) hydromorphone is released after 1 hour, from 25% to 65% (by wt) hydromorphone is released after 2 hours, from 45% to 85% (by wt) hydromorphone is released after 4 hours and greater than 60% (by wt) hydromorphone is released after 8 hours, and (ii) the in-vitro release rate is substantially independent of pH in that a difference, at any given time, between an amount of hydromorphone released at one pH and an amount released at any other pH, when measured in-vitro using the

USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,

the dosage form providing a duration of therapeutic effect of at least 24 hours and a mean C_{max} of hydromorphone from about 1070 pg/ml to about 1721 pg/ml and a T_{max} of between 4.6 and 8 hours, based on a single dose administration of the dosage form comprising 8 mg of hydromorphone hydrochloride.

Claim 7. (Previously Presented): The method of claim 6, wherein said dosage form comprises a pharmaceutically acceptable salt of hydromorphone.

Claim 8. (Previously Presented): The method of claim 6, wherein said dosage form comprises hydromorphone hydrochloride.

Claims 9-12. (Cancelled)

Claim 13. (Currently Amended): The method of claim 6, wherein the controlled release formulation <u>further</u> comprises a polymer selected from the group consisting of a pharmaceutically acceptable gum, an alkylcellulose, a cellulose ether, an acrylic resin, and mixtures of the foregoing.

Claim 14. (Previously Presented): The method of claim 13, wherein the controlled release formulation further comprises a digestible substituted or unsubstituted C_8-C_{50} hydrocarbon.

Claim 15. (Previously Presented): The method of claim 14, wherein said hydrocarbon is selected from the group consisting of fatty acids, fatty alcohols, mineral oils, vegetable oils, waxes and mixtures of any of the foregoing.

Claim 16. (Previously Presented): The method of claim 13, wherein said dosage form further comprises a polyalkyleneglycol.

Claims 17-23. (Cancelled)

Claim 24. (Currently Amended): A method for treating pain in humans for a time period of about 24 hours, comprising

administering to a human patient at a dosing interval of about 24 hours a solid, controlled-release oral dosage form comprising an active agent consisting essentially of 8 to 64 mg of hydromorphone or a pharmaceutically acceptable salt thereof incorporated into a controlled-release formulation comprising a tablet overcoated with a controlled-release coating derived from an aqueous dispersion of a hydrophobic polymer selected from the group consisting of a cellulosic polymer, an acrylic polymer, and mixtures thereof,

wherein the coating has been stabilized by curing for about 24 hours or more at a temperature greater than the glass transition temperature of the hydrophobic polymer and a relative humidity from about 60% to about 100% such that the dosage form attains a dissolution profile which is substantially unaffected by exposure to storage conditions of at least one month at a temperature of 40°C and a relative humidity of 75%,

wherein (i) the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C, is such that from 12.5% to 42.5% (by wt) hydromorphone is released after 1 hour, from 25% to 65% (by wt) hydromorphone is released after 2 hours, from 45% to 85% (by wt) hydromorphone is released after 4 hours and greater than 60% (by wt) hydromorphone is released after 8 hours, and (ii) the in-vitro release rate is substantially independent of pH in that a difference, at any given time, between an amount of hydromorphone released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,

the dosage form providing a duration of therapeutic effect of at least 24 hours, a mean C_{max} of hydromorphone from about 1070 pg/ml to about 1721 pg/ml and a T_{max} of between 4.6 to

8 hours, based on a single dose administration of the dosage form comprising 8 mg of hydromorphone hydrochloride.

Claim 25-26 (Cancelled)

Claim 27. (Previously Presented): The method of claim 6, wherein the dosage form provides a peak plasma level of hydromorphone obtained in-vivo which occurs between 4.8 to 8 hours after administration of the dosage form.

Claim 28. (Previously Presented): The method of claim 24, wherein the dosage form provides a peak plasma level of hydromorphone obtained in-vivo which occurs between 4.8 to 8 hours after administration of the dosage form.

Claim 29. (Previously Presented): The method of claim 6, wherein the dosage form provides a peak plasma level of hydromorphone obtained in-vivo which occurs between 5.5 to 8 hours after administration of the dosage form.

Claim 30. (Previously Presented): The method of claim 24, wherein the dosage form provides a peak plasma level of hydromorphone obtained in-vivo which occurs between 5.5 to 8 hours after administration of the dosage form.

Claim 31. (Previously Presented): The method of claim 6, wherein the dosage form provides the mean C_{max} of hydromorphone of 1211 ± 153 pg/ml.

Claim 32. (Previously Presented): The method of claim 6, wherein the dosage form provides a mean C_{24} of hydromorphone of about 600 pg/ml.

Claim 33. (Previously Presented): The method of claim 24, wherein the dosage form provides the mean C_{max} of hydromorphone of 1211 ± 153 pg/ml.

Claim 34. (Previously Presented): The method of claim 24, wherein the dosage form provides a mean C_{24} of hydromorphone of about 600 pg/ml.

Claim 35. (Currently Amended): A method for treating pain in humans for a time period of about 24 hours, comprising

administering to a human patient at a dosing interval of about 24 hours a solid, controlled-release oral dosage form comprising 8 to 64 mg of hydromorphone or a pharmaceutically acceptable salt thereof incorporated into a controlled-release formulation comprising a tablet overcoated with a controlled-release coating derived from an aqueous dispersion of a hydrophobic polymer selected from the group consisting of a cellulosic polymer, an acrylic polymer, and mixtures thereof, and a barrier coating separating hydromorphone from the controlled-release coating,

wherein (i) the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C, is such that from 12.5% to 42.5% (by wt) hydromorphone is released after 1 hour, from 25% to 65% (by wt) hydromorphone is released after 2 hours, from 45% to 85% (by wt) hydromorphone is released after 4 hours and greater than 60% (by wt) hydromorphone is released after 8 hours, and (ii) the in-vitro release rate is substantially independent of pH in that a difference, at any given time, between an amount of hydromorphone released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,

the dosage form providing a duration of therapeutic effect of at least 24 hours, a mean C_{max} of hydromorphone of from about 1070 pg/ml to about 1721 pg/ml and a T_{max} of between 4.4 and 8 hours, based on a single dose administration of the dosage form comprising 8 mg of hydromorphone hydrochloride.

Claim 36 (Previously Presented): The method of claim 35, wherein the dosage form provides a mean C_{max} of 1211±153 pg/ml.

Claim 37 (Currently Amended): A method for treating pain in humans for a time period of about 24 hours, comprising

administering to a human patient at a dosing interval of about 24 hours a solid, controlled-release oral dosage form comprising an active agent consisting essentially of 8 to 64 mg of hydromorphone or a pharmaceutically acceptable salt thereof incorporated into a controlled-release formulation comprising a tablet overcoated with a controlled-release coating derived from an aqueous dispersion of a hydrophobic polymer selected from the group consisting of a cellulosic polymer, an acrylic polymer, and mixtures thereof,

wherein the coating has been stabilized by curing for about 24 hours or more at a temperature greater than the glass transition temperature of the hydrophobic polymer and at a relative humidity from about 60% to about 100% such that the dosage form attains a dissolution profile which is substantially unaffected by exposure to storage conditions of at least one month at a temperature of 40°C and a relative humidity of 75%,

wherein (i) the dissolution rate in vitro of the dosage form, when measured by the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm at 900 ml aqueous buffer at pH 1.6 and 7.2 and at 37°C, is such that from 12.5% to 42.5% (by wt) hydromorphone released after 1 hour, from 25% to 65% (by wt) hydromorphone released after 2 hours, from 45% to 85% (by wt) hydromorphone released after 4 hours and greater than 60% (by wt) hydromorphone released after 8 hours, and (ii) the in-vitro release rate is substantially independent of pH in that a difference, at any given time, between an amount of hydromorphone released at one pH and an amount released at any other pH, when measured in-vitro using the USP Paddle Method of U.S. Pharmacopeia XXII (1990) at 100 rpm in 900 ml aqueous buffer is no greater than 10%,

the dosage form providing a duration of therapeutic effect of at least 24 hours, a mean C_{max} of hydromorphone from about 1070 pg/ml to about 1721 pg/ml and a T_{max} of between 4.4 to 8 hours, based on a single dose administration of the dosage form comprising 8 mg of hydromorphone hydrochloride.

Claim 38 (Previously Presented): The method of claim 37, wherein the dosage form provides a mean C_{max} of hydromorphone of 1211±153 pg/ml.

Claim 39 (Previously Presented): The method of claim 6, wherein the controlled-release formulation further comprises a barrier coating separating hydromorphone from the controlled-release coating.

Claim 40 (Previously Presented): The method of claim 24, wherein the controlled-release formulation further comprises a barrier coating separating hydromorphone from the controlled-release coating.

Claim 41 (Previously Presented): The method of claim 37, wherein the controlled-release formulation further comprises a barrier coating separating hydromorphone from the controlled-release coating.

Claim 42-43 (Cancelled)